

XARELTO® (rivaroxaban tablets) in Knee and Hip Replacement Surgery

Fast Facts:

- XARELTO® is a novel, once-daily, oral anticoagulant recently approved in the United States for the prevention (prophylaxis) of deep vein thrombosis (DVT) which may lead to a pulmonary embolism (PE) in patients undergoing knee or hip replacement surgery.
- XARELTO® is a Factor Xa inhibitor, and works by selectively blocking the blood clotting Factor Xa in the blood clotting cascade to reduce the tendency of blood to form clots.¹
- Blood clots form to prevent prolonged bleeding in response to damage to a blood vessel; they act as a plug at the site of the blood vessel injury.
- Certain surgical procedures may increase the risk of inappropriate activation of the blood clotting cascade that can lead to the formation of potentially fatal blood clots.
- Venous blood clots (also known as venous thromboembolism, or VTE) are a major health problem, causing approximately 300,000 deaths in the U.S. each year.²
- VTE can take the form of either:
 - A deep vein thrombosis (DVT): a blood clot in a deep vein (usually in the leg) that partially or totally blocks the flow of blood which may lead to;
 - A pulmonary embolism (PE): a blood clot in the lungs that can partially or totally block the flow of blood.
- People at risk of venous blood clots include healthy people undergoing major orthopedic surgery (total knee and hip replacement surgeries).

About VTE

VTE is a potentially deadly condition caused by abnormal (pathologic) blood clots that form in the veins. VTE includes deep vein thrombosis (DVT) and pulmonary embolism (PE).

DVT occurs when blood clots in one of the large, deep veins in the legs. Larger blood clots that substantially block the flow of blood may cause pain and swelling in the affected leg. Other symptoms can include redness and feeling of warmth in the leg.³ Blood clots that only partially block the flow of blood often produce no symptoms; these asymptomatic episodes account for approximately half of all DVT cases.⁴ Studies suggest that approximately 50% of patients with untreated proximal DVT – which are specifically in the deep knee or thigh veins – will develop symptomatic PE within 3 months.⁵

Pulmonary embolism (PE) is a serious, potentially life-threatening complication of DVT.⁶ A PE most commonly occurs when part or all of a deep venous clot dislodges from the vein where it originated, and is then carried along with the venous blood flow through the right chamber of the heart and into the pulmonary arterial circulation, where it can partially or completely block a branch of the pulmonary artery. Typically, PE causes shortness of breath, rapid breathing, rapid heart rate, sweating, and chest pain.⁷ Some patients cough up blood, while others faint. When PE occurs with large clots, or multiple clots, or when the patient already has preexisting heart or lung disease, the process may be rapidly fatal.⁸

Healthcare costs associated with venous blood clots

Complications associated with VTE and its treatment are frequent and costly. The main drivers of VTE costs are initial and recurrent medical events – or their associated complications – requiring hospitalization.⁹

In the U.S., DVT and PE costs for initial hospitalization average more than \$9,800 and \$14,000, respectively; rehospitalization costs average more than \$11,800 and \$14,700, respectively.⁹ In light of the high overall costs of treatment, using effective VTE prevention strategies after major orthopedic surgery could reduce the economic burden of VTE.

VTE following knee or hip replacement surgery

Osteoarthritis is the number one driver for patients to opt for knee or hip replacement surgery, and usually occurs in people over the age of 50.¹⁰ Patients undergoing major orthopedic surgery are at high risk for VTE. In the U.S., more than 800,000 people have hip and knee replacement surgery each year, and the most common preventable complications are venous blood clots.^{10,11} With an aging population in the U.S., the demand for hip and knee replacement surgeries is expected to rise by 174% and 673%, respectively, by 2030.¹²

Venous blood clots occur in 40-60% of patients undergoing orthopedic surgery who do not receive preventive care.¹³ The American College of Chest Physicians (ACCP) has recommended extended anticoagulation prophylaxis to help reduce the occurrence of DVT or PE following knee or hip replacement surgery.¹³

About XARELTO®

To date, XARELTO® is approved in more than 110 countries worldwide and has been successfully launched by Bayer HealthCare in more than 80 countries including Australia, Canada, China, Mexico and within the European Union for the prevention of VTE in adult patients undergoing elective hip or knee replacement surgery. Janssen Pharmaceuticals, Inc. holds marketing rights for XARELTO® in the U.S.

Important Safety Information

WHAT IS XARELTO®?

- XARELTO®(rivaroxaban tablets) is a prescription medicine used to help prevent blood clots from forming in patients after hip or knee replacement surgery.

WHAT IS THE MOST IMPORTANT INFORMATION I SHOULD KNOW ABOUT XARELTO®?

- You should take XARELTO® exactly as directed by your doctor
- Do not skip a dose or stop taking XARELTO® unless you are advised to do so by your doctor. Stopping may increase your risk of a blood clot

- If a dose is missed, take XARELTO as soon as possible and continue on the following day, taking XARELTO® as directed by your doctor. Do not take two doses at the same time
- XARELTO® can cause bleeding, which can sometimes be serious, even life-threatening. You may find you bruise or bleed more easily while you take it. It might take longer than usual to stop bleeding
- Alert your doctor right away if you develop any:
 - Tingling, numbness or muscle weakness, especially in your legs. This is particularly important if you had a procedure called spinal or epidural puncture as part of your anesthesia for your hip or knee replacement surgery.
 - Unusual bleeding or bruising (bruises that develop without an injury or grow in size)
 - New bleeding (for example, nose bleeds, bleeding gums, red urine, bright red blood in your stool, coughing up or vomiting blood)
 - Bleeding that is heavier than usual (for example, from cuts or menstruation)
 - Dizziness, weakness, or tiredness, all of which could indicate a loss of blood
 - Pain, swelling, or new fluid leakage in or around the surgical incision

WHO SHOULD NOT TAKE XARELTO®?

Tell your doctor if you have:

- Unusual bleeding
- Ever had an allergic-type (hypersensitivity) reaction to XARELTO®

WHAT SHOULD I TELL MY DOCTOR BEFORE OR WHILE TAKING XARELTO®?

- Tell your doctor or dentist about all the medicines you take.
 - This includes XARELTO®, any other prescription and nonprescription medicines, over-the-counter medications, and herbal supplements.
- Tell your doctor if you:
 - Have a bleeding disorder or have problems with unusual bleeding
 - Have any problems with your kidneys or liver

- o Are pregnant or planning to become pregnant.
- o Are breast-feeding or are planning to breast-feed

WHAT ARE THE POSSIBLE SIDE EFFECTS OF XARELTO®?

- XARELTO® may increase your chance of bleeding. This bleeding can sometimes be serious (and even life-threatening)
- In studies side effects with XARELTO® included fluid leakage from a wound, itching, pain in arms or legs, blisters, fainting, and muscle spasm.
- **Discuss any side effects with your doctor. You are also encouraged to report side effects to the FDA: visit <http://www.fda.gov/medwatch> or call 1-800-FDA-1088.** You may also report side effects to Janssen Pharmaceuticals, Inc. at 1-800-JANSSEN (526-7736)

This is a summary of important information about XARELTO®. If you would like more information, talk with your doctor.

Please see full Product Information, or visit www.XARELTOhcp.com.

References:

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